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September 29, 2000

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 10-61
Rockville, Maryland 20857

Re: Petition for Stay of Action – Approval of ANDAs for Cefuroxime Axetil Products Not Containing the Same Active Ingredient as Ceftin® Products, *i.e.*, Not Containing Strictly the Amorphous Form of the Drug Substance

Dear Sir or Madam:

PETITION FOR STAY OF ACTION

We are submitting this Petition for Stay of Action on behalf of Glaxo Wellcome Inc. ("GW"), which markets cefuroxime axetil as Ceftin® Tablets and Ceftin® for Oral Suspension. Simultaneously with this Petition for Stay of Action, we are filing a Citizen Petition that asks the Food and Drug Administration ("FDA") to decline to approve any new or pending abbreviated new drug application ("ANDA") or application submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for any generic cefuroxime axetil product that contains cefuroxime axetil in crystalline form and, if FDA nevertheless were to evaluate such a product, that asks FDA to require that any formulation including crystalline cefuroxime axetil be approved only subject to tight drug product and drug substance specifications controlling for solid state form, including the content of individual polymorphs. In this Petition, GW requests that the Commissioner of Food and Drugs stay the approval of any approved application or decision to approve any new or pending application for a product that includes cefuroxime axetil in crystalline form until final resolution of the issues raised in the Citizen Petition.

A. Decision involved

Presently before the FDA is the question whether the Agency may approve or maintain approval of ANDAs or section 505(b)(2) applications for generic cefuroxime axetil products if the formulation includes crystalline cefuroxime axetil, as well as the testing and controls that should be required if such a product were approved. This depends on the issues addressed by the Citizen Petition submitted on the same date as this Petition for Stay of Action.

B. Action requested

In this Petition for Stay of Action, GW requests that FDA stay approval of all new or pending ANDAs or section 505(b)(2) applications for cefuroxime axetil products for which the formulation includes cefuroxime axetil in crystalline form. GW requests that the stay continue until resolution of the issues raised by the accompanying Citizen Petition. Should FDA deny that Citizen Petition, GW asks that the stay requested herein not expire until a reviewing court has ruled on the correctness of that decision so long as GW seeks court review within two weeks of its receipt of the adverse decision.

Based on publicly available information, including information available on FDA's web-site concerning Drug Master Files and the publication of a proposed revision to the United States Pharmaceopeia (U.S.P.) monograph on cefuroxime axetil, GW believes that at least one ANDA (for a formulation including crystalline cefuroxime axetil) may be pending at FDA and that FDA may be considering approval of such an application. Because of the necessity for quick review in these circumstances, GW specifically requests a grant of this Petition for Stay of Action by October 31, 2000. Any failure by the FDA to act on this Petition within that time will, accordingly, constitute the denial of this aspect of this Petition.

C. Statement of grounds

The accompanying Citizen Petition demonstrates that the marketing of generic cefuroxime axetil products including the crystalline form of the drug substance would be contrary to law and could, because of the inherent quality issues, present a risk to the public health. Accordingly, it is crucial that such ANDAs not be approved unless FDA has resolved the issues presented by the Citizen Petition, and if those issues are resolved against GW, until GW has an opportunity for judicial review of that decision.

There is precedent for granting stays where, as here, significant legal and policy issues have been raised about FDA policies. *See, e.g.*, 45 Fed. Reg. 82,052 (Dec. 12,

1980) (reference to stay of "paper NDA" policy until 10 days after denial of citizen petition challenging that FDA policy).

This Petition for Stay of Action satisfies the prerequisites for a mandatory grant of a stay under FDA regulations. *See* 21 C.F.R. § 10.35(e)(1)-(4).

The petitioner will otherwise suffer irreparable injury. Here, GW will face diminution of the reputation of its Ceftin® products if generic products with different quality characteristics are approved and marketed. This injury would be even greater should adverse events result from the quality differences. In addition, GW will lose sales of its Ceftin® products to generic products once they are marketed. There is no mechanism by which the harm to GW, if it occurs, can be repaired.

The petitioner's case is not frivolous and is being pursued in good faith. The accompanying Citizen Petition illustrates that the petitioner's case is not frivolous and is well grounded in applicable law. This matter is being pursued in good faith, with every attempt being made to seek resolution in an appropriate and expeditious manner based on the application of applicable law to the facts presented.

The petitioner has demonstrated sound public policy grounds supporting the stay. As FDA is aware, the current U.S.P. monograph, the labeling for Ceftin®, the former antibiotic monograph for cefuroxime axetil, and indeed the very approval of Ceftin®, were all based on clinical experience demonstrating the efficacy of cefuroxime axetil products containing exclusively amorphous drug substance. Permitting the marketing of products containing crystalline drug substance would be contrary to governing law and would, unless significant testing were performed and tight acceptance criteria adopted, potentially put patients at risk. GW has tried to engage FDA more informally on this issue through the channels of scientific exchange and dialogue. The issue is clearly a significant one, whose prompt resolution is important to all concerned. A stay until FDA responds to GW's Citizen Petition addressing the questions raised is certainly justified.

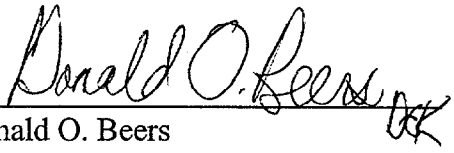
The delay resulting from the stay is not outweighed by public health or other public interest. Once the issues presented by the Citizen Petition are addressed by FDA, petitioner is confident that FDA will conclude that generic cefuroxime axetil products should be limited to the amorphous drug substance. There is no public interest in the marketing of products that are not clinically the same as the innovator product. At a time of rising concern about the public health threat posed by the emergence of microbial resistance to antibiotics, the potential for compromised product quality and efficacy is all the more serious. *See* "Proposed Rule: Labeling Requirements for Systemic Antibacterial Drug Products Intended for Human Use," 65 Fed. Reg. 56,511 (Sept. 19, 2000). More

generally, there can, of course, be no public interest in having FDA rush into inappropriate approvals, without considering concerns that are scientifically valid and medically relevant to the propriety of those approvals.

Even were FDA not to find that the criteria for mandatory stay discussed above had been satisfied, such a stay should be granted under the Agency's discretionary authority to stay any action "in the public interest and in the interest of justice." 21 C.F.R. § 10.35(e). The issues raised by GW's Citizen Petition are clearly substantial. The interests of the public and of justice demand a fair and expeditious resolution of those issues in an orderly process.

For the reasons stated above, GW asks that the requested stay be entered as soon as possible and no later than October 31, 2000.

Respectfully submitted,



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